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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/325,095	06/03/99	HILES I	LUD5246.4JEL

EXAMINER
HINES, I

ART UNIT	PAPER NUMBER
1645	13

DATE MAILED: 09/13/01

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HM12/0913

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

File Copy

Office Action Summary

Application No.	Applicant(s)
09/325,095	Hiles et al.
Examiner	**Art Unit**
Ja-Na Hines	1645

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Jun 25, 2001*.

2a) ☒ This action is FINAL. 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *39-50* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *39-50* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☐ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
18) ☐ Interview Summary (PTO-413) Paper No(s). _____
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other:

DETAILED ACTION

Amendment Entry

1. The amendment filed June 25, 2001 has been entered. Claims 27-38 have been canceled. Claims 39-50 have been newly added.

Pending Claims

2. Claims 39-50 are pending in this Office Action.

Drawings

3. Applicant is required to submit a proposed drawing correction in reply to this Office action as cited on the PTO-form 948. However, formal correction of the noted defect can be deferred until the application is allowed by the examiner.

Claim Objections

4. Claim 47 is objected to because of the following informalities: Claim 47 uses the word "hypridizes." Claims 39, 47 and 48 recite 1M NaCl, and 10 mM EDTA. These appear to be mistakes, therefore appropriate correction is required. If not, then an explanation is appropriate.

Withdrawal of Rejections

5. Claim 36 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn in view of applicants amendments.

6. Claims 27-35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Skolnik et al., in view of Carpenter et al., is withdrawn in view of applicants newly entered claims.

New Grounds for Rejections

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 39-50 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. Claims 39, 47 and 48 recite hybridization conditions, however the conditions recited in the claims are not supported by the data in the specification. For instance, on page 40 of the specification, the hybridization procedure uses 1M NaCl, and 10 mM EDTA and not 1mNaCL and 10mMEDTA as recited in the claims. The reagents in the specification are individual reagents, however the claims recite the reagents in a format which appears to make the reagents divisible by one another. Finally, the specification recites multiple washing steps in the alternative, however the claims recite all washing steps as consecutive. Therefore, the

hybridization procedures in the claims constitute new matter, since the procedures as recited are not taught in the specification.

8. Claim 48 is rejected because it recites comparing hybridization increases and decreases to determine whether the substance is an antagonist or agonist, however no support for the recited method and comparisons can be found in the specification. Applicant has not pointed to specific sections in the specification to indicate where support can be found. Thus the new claims recite method steps not recited in the specification or original claims, therefore the claims are rejected as containing new matter.

9. Claims 39-50 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claims set forth the nucleic acid molecules recited in SEQ ID NO: 12, 14-18, 21-22, 24-25, 27 and 29. However neither the specification nor the claims teach how to define the variables G, H, Y or W, as recited within the sequences.

Vas-Cath Inc. V. Mahurkar, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117). The specification does not "clearly allow persons of

ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116).

Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision (see page 115). Thus, the structure of nucleic acid molecules is not defined. Even though claims 44-45 recite sequence identification numbers, the skilled artisan cannot envision the detailed structure of the encompassed nucleic acid molecules since the specification has not defined what the variable can be. Therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method for determining expression. Adequate written description requires more than a mere statement that it is part of the invention and a reference to a potential method of expression. The nucleic acid itself is required. See *Fiers v. Revel*, 25 USPQ 2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Lts.*, 18 USPQ2d 1016.

Furthermore, *In The Reagents of the University of California v. Eli Lilly*, (43 USPQ2d 1398-1412), the court held that a generic statement which defines a genus of nucleic acids does not provide an adequate written description of the genus. Applicants are not required to disclose every species encompassed by a genus, thus the description of a genus is achieved by the recitation of a representative number of SEQ ID NO's, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a nucleic acid molecule...'requires a precise definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention".

However, the sequences identified in the claims do not set forth a precise definition of the sequence. No disclosure as to the identity of the variables, beyond the mere mention of their existence in the nucleic acid molecules in the response of June 25, 2001 is made. This is insufficient to support the generic claims as provided by the Interim Written Description Guildlines published in the June 15, 1998 Federal Register at Volume 63, Number 114, pages 32639-32645.

Therefore, the full breadth of the claims fails to meets the written description provision of 35 USC 112, first paragraph.

10. Claims 39-50 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The claims are drawn to a method of determining expression; a method of determining if a cell contains a gene; or a method for determining if a substance is an agonist or antagonist, however neither the claims nor the specification teach methods for determining expression, determining if a cell contains a gene or determining if a substance is an agonist or antagonist.

Many nucleic acid molecules that hybridize to a transcript of the gene will not be an indicator of a human polypeptide having PI3 kinase activity and a molecular weight of about 110kD as determined by SDS-PAGE. Neither does hybridization determine whether a cell contains a gene which encodes a human polypeptide which has PI3 kinase activity and have a

molecular weight of 110kD as determined by SDS-PAGE. The specification does not even recite the use of nucleic acid sequences set forth in SEQ ID NO: 12, 14-18, 21-22, 24-25, 27 and 29 or how to define the variables recited within them.

The claims broadly teach contacting a sample with a nucleic acid molecule which hybridizes to a transcript gene, thus any nucleic acid molecule is being claimed, where no specific nucleic acid molecule is recited and the specific hybridization conditions are of low or no stringency. No specific methods of determination are taught or enabled by the specification. Applicants have provided no guidance to enable one of ordinary skill in the art how to determine without undue experimentation the method for determining gene expression using every single nucleic acid molecule that could possibly hybridize to the transcript gene.

The specification does not provide guidance on how any nucleic acid molecule can be used to hybridize and then encode a human polypeptide with the recited criteria. No working examples are shown containing the missing information. Without such information, one of skill in the art could not predict which nucleic acid molecules would hybridize to the transcript gene, neither can one predict the method of expression which results in an encoded human polypeptide.

Accordingly, one of skill in the art would be required to perform undue experimentation to use any nucleic acid molecule to determine the expression of a gene without any specifically recited hybridizing conditions. Therefore, one skilled in the art could not make and/or use the invention without undue experimentation.

11. Claims 39-50 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 39-50 are again rejected for requiring the use of a nucleic acid molecule in a sample, however the nucleic acid molecule is undefined. The nucleic acid molecule is indefinite because it recites no limitations. Claims 39, 47 and 48 broadly recite any nucleic acid molecule since the nucleic acid molecule is not defined by a particular sequence. Furthermore, claims 44 and 45 recite specific nucleic acid molecules, however the nucleic acid sequences include undefined variables. See also the related 112 1st rejections.

12. Claims 39-50 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MEP. § 2172.01. The omitted steps are: There is no contact step, no detection step and no correlation step which correlates the detection to the method of determining expression of gene which encodes a human polypeptide with PI3 kinase activity and an molecular weight of 110kD. The steps in the claim are drawn to the hybridization procedure and not to the method of: determining expression, determining if a cell contains a gene or determining if a substance is an agonist or antagonist. The hybridization steps in the claims merely recite low or non stringent requirements. The claims do not recite any method to achieve a method of determining expression, a method of determining if a cell contains a gene or a method for determining if a substance is an agonist or antagonist.

Previous Grounds for Rejections Maintained

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

13. Claims 39-47 and 49-50 are rejected under 35 U.S.C. 103(a) as being unpatentable over Skolnik et al., in view of Carpenter et al., is maintained. It is understood that applicant has submitted new claims however, claims 39-47 and 49-50 are rejected under 35 U.S.C. 103(a) as being unpatentable over Skolnik et al., in view of Carpenter et al. Skolnik et al., in view of Carpenter et al., have been discussed in detail in the Office Action dated October 12, 1999.

Response to Arguments

14. Applicant's arguments filed May 25, 2001 have been fully considered but they are not persuasive.

Applicant argues that the claims relate to nucleic acid hybridization assays and that it is not seen how the 110kD protein of Carpenter in the method of Skolinik would have rendered the invention obvious. However the claims recite a method for determining expression of a gene which encodes a polypeptide that has PI-3 kinase activity. Skolnik et al., teaches the cloning of PI3 kinase and a novel method for expression and cloning of target proteins. The GRB-1 protein encodes the human counterpart of PI3 kinase -associated protein p85 which is a polypeptide that has PI-3 kinase activity. The claims recite contacting a sample with an undefined nucleic acid

molecule which hybridizes to the transcript of the gene. Skolnik et al., teach the determination and detection of binding the EGFR to an SH2-containing protein. The EGFR domain could bind specifically to an SH2-containing protein.

Finally, Skolnik et al., teach hybridization procedures. Thus Skolnik et al., teach a method for determining gene expression.

In response to applicant's argument that there is no suggestion to combine the references, and it is unclear what substitution is proposed, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988)and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, no more than routine skill would have been required to have used the 110kD protein as taught by Carpenter et al., instead of the 85kD protein of Skolnik et al. One having ordinary skill in the art would have been motivated to make such a change as a mere alternative or functionally equivalent protein. The prior art clearly teaches gene expression and hybridization techniques. The use of an alternative protein, such as the 110 kD would have been desirable to those of ordinary skill in the art because Carpenter et al., teach that the 110 kD protein was isolated by SDS-PAGE, is correlated to the PI3 kinase activity, strongly related to cell growth activity, its gene products can be found of different genes and it is crucial in intracellular signals which respond to a number of hormones and growth factors.

Sequence Compliance

15. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. § 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 C.F.R. §§ 1.821-1.825 for the reason set forth: The specification at pages 38-39, 41, and 52-53 recites sequences without reciting the corresponding sequence identifying numbers. It appears as if the sequences correspond to SEQ ID NO: 20-25. Therefore applicant is asked to amended the specification to include the appropriate SEQ ID NO's for all sequences without a sequence identifying number. Applicant is therefore asked to comply with the sequence compliance rules.

APPLICANT IS GIVEN THE TIME WITHIN THE APPLICATION TO COMPLY WITH THE SEQUENCE RULES, 37 C.R.F. §§ 1.821-1.825. Failure to comply with these requirements will result in ABANDONMENT of the application under 37 C.F.R. § 1.821(g). Extensions of time may be obtained by filing a petition accompanied by the extension fee under the provisions of 37 C.F.R. § 1.136. In no case may an applicant extend the period for response beyond the six month statutory period. Direct the response to the undersigned. Applicant is requested to return a copy of the attached Notice to Comply with the response.

16. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ja-Na Hines whose telephone number is (703) 305-0487. The examiner can normally be reached on Monday through Thursday from 6:30am to 4:00pm. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached on (703) 308-3909. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Ja-Na Hines

August 27, 2001

LYNETTE R. F. SMITH
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

Application No.: 09/325,095

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

Applicant must file the items indicated below within the time period set the Office action to which the Notice is attached to avoid abandonment under 35 U.S.C. § 133 (extensions of time may be obtained under the provisions of 37 CFR 1.136(a)).

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

- [X] 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). If the effective filing date is on or after July 1, 1998, see the final rulemaking notice published at 63 FR 29620 (June 1, 1998) and 1211 OG 82 (June 23, 1998).
- [ ] 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).
- [ ] 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).
- [ ] 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."
- [ ] 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).
- [ ] 6. The paper copy of the "Sequence Listing" is not the same as the computer readable from of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).
- [X] 7. Other: The specification recites sequences not identified by a sequence indentifying number.

Applicant Must Provide: (Should a new CRF be necessary for sequences not in the raw sequnce listing)

- [X] An initial or substitute computer readable form (CRF) copy of the "Sequence Listing"
- [X] An initial or substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification.
- [X] A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (703) 308-4216
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